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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,660

09/28/2006

Satoshi Amano

27563U

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20529 7590 11/23/2010
THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314

EXAMINER

GHALI, ISIS A D

ART UNIT

PAPER NUMBER

1611

MAIL DATE

DELIVERY MODE

11/23/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/587,660	Applicant(s) AMANO ET AL.	
	Examiner Isis A. Ghali	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7,8 and 11-15 is/are pending in the application.
- 4a) Of the above claim(s) 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7,8 and 11-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The receipt is acknowledged of applicants' amendment filed 09/15/2010.

Claims 7-15 previously presented. Claims 9-10 are currently canceled.

Claims 7-8, 11-15 are pending.

1. Claim 15 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was considered as made **without** traverse in the reply filed on 4/23/2010.

Claims 7-8, 11-14 are included in the prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

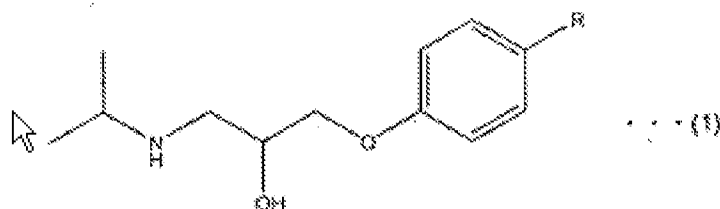
5. Claims 7-8, 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanios et al. US 6,905,016, in view of JP 2003-313122 ('122), or *vice versa*, JP '122 in view of Kanios.

Applicant Claims

Applicant currently amended claims 7 recites a patch-containing pouch housing in its interior a patch which has a pressure-sensitive adhesive layer laminated on at

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least one side of a support and has a release film attached to said pressure-sensitive adhesive layer, wherein said pressure-sensitive adhesive layer contains a drug represented by general formula (1)



or a pharmaceutically acceptable salt thereof, wherein R represents 2-isopropoxyethoxymethyl, carbamoylmethyl or 2-methoxyethyl, and wherein at least a portion of the inner surface of said pouch in contact with said patch is made of polyacrylonitrile.

The claimed compound is bisoprolol.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

Kanios teaches package for transdermal system to prevent and control degradation reactions that resulting from contamination of active material with packaging materials and improves stability of the drug during storage prior to use (abstract; col.3, lines 58-67; col.4, lines 18-22). The package material is inert to the component of the transdermal system (col.4, lines 27-30). Figure 1 shows the package material is multi-layered including layer 11 the innermost layer adjacent to the transdermal system and layer 12 the outermost layer distant from the transdermal system. The preferred packaging material for layer 11 does not react with or otherwise

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adversely affect the drug or other components of the transdermal system. Preferred material for layer 11 is acrylonitrile. Preferred material to layer 12 is polyester or laminate comprising Mylan polyester and aluminum foil, Mylan is polyethylene terephthalate. (See col.6, lines 21-67). The thickness of layer 11 is from 0.5 mil to 2.5 mil and the thickness of layer 12 is from 0.2 to 3.0 mil (col.6, lines 34-55) which is equivalent to 12.7-63 μm for layer 11 and 5-76 μm for layer 12. This teaching implies that the thickness of the multilayer film is from 17.7 to 139 μm and the reference suggested thinner and thicker widths may be employed. Active agents suitable for delivery by the packaged transdermal system includes propranolol (col.8, line 45).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

Although Kanios teaches propranolol as active agent suitable for transdermal system, however, Kanios does not teach bisoprolol as instantly claimed by claim 7, or the adhesives claimed by claim 8.

JP '122 teaches patch to deliver bisoprolol transdermally comprising adhesive layer containing bisoprolol or its pharmaceutically acceptable salts, support layer and release liner (abstract; paragraph 0023, 0032). The adhesive is acrylate-based adhesive including acrylic acid that has increased release of the drug from the adhesive and high percutaneous absorption for prolonged period with reduced irritation and residue on the skin (paragraphs 0005, 0007-0011). Bisoprolol is highly selective β_1

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receptor antagonist and effective to treat essential hypertension and angina and to improve arrhythmia (paragraph 0002).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a package for a transdermal system comprising innermost layer of acrylonitrile and outermost layer of polyethylene terephthalate forming multilayer film having thickness between 17.7 to 139 μm as taught by Kanios wherein the patch used to deliver propranolol, and replace propranolol with bisoprolol in adhesive comprising acrylic acid as taught by JP '122. One would have been motivated to do so because JP '122 teaches that bisoprolol is highly selective β_1 receptor antagonist and effective to treat essential hypertension and angina and to improve arrhythmia, and one would have used acrylic acid based adhesive taught by JP '122 because JP '122 teaches that such adhesive has increased release of the drug from the adhesive and high percutaneous absorption for prolonged period with reduced irritation and residue on the skin. One would reasonably expect formulating transdermal system comprising acrylic acid-based adhesive layer containing bisoprolol wherein the patch is packaged in a multilaminate package having the innermost layer of acrylonitrile and outermost layer of polyethylene terephthalate, and wherein the patch is stabilized during storage, provides high drug release and skin absorption for long period during use and effectively treat essential hypertension and angina and to improve arrhythmia.

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Vise versa, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal patch to deliver bisoprolol comprising acrylic acid-based adhesive layer containing bisoprolol, support layer and release liner as taught by JP '122, and further pack the patch in the multilaminate package taught by Kanios comprising innermost layer adjacent to the transdermal system made of polyacrylonitrile and outermost layer distant from the transdermal system made of polyethylene terephthalate forming multilayer film having thickness between 17.7 to 139 μm . One would have been motivated to do so because Kanios teaches such a package prevents and controls degradation reactions that resulting from contamination of active material with packaging materials and improves stability of the drug during storage prior to use. One would reasonably expect formulating stable transdermal system comprising acrylic acid-based adhesive layer containing bisoprolol wherein the patch is packaged in a multilaminate package having the innermost layer of acrylonitrile and outermost layer of terephthalate, and wherein the patch is protected against degradation reactions that resulting from contamination of active material with packaging materials.

Regarding the claimed amounts thickness of the multilayered film, Kanios teaches 17.7-139 μm and the present claims recite 20-100 μm . Therefore, the thickness taught by the prior art overlaps with the instant claims. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. **See MPEP 2144.05 [R-5].**

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

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instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

6. Applicant's arguments filed 09/15/2010 have been fully considered but they are not persuasive.

Applicants argue that a proper case of prima facie obviousness has not been established because whether taken alone, or in combination, none of the cited references teach or suggest every element of the presently claimed subject matter, specifically the thickness of the multilayer film of from 20 to 100 μm , which is of about 10 to 62 times less than that taught by Kanios having a total thickness of about 1000 to 6250 μm . In addition, JP '122 merely describes bisoprolol containing patch. Applicants argue that the presently claimed subject matter is unexpectedly superior over the cited art for at least the reason that the presently claimed pouch has a thickness much less than the pouches in the cited art, but is still an effective storage system for a patch containing an active ingredient, which has superior gas permeability and manageability.

In response to these arguments, it is argued that Kanios teaches the thickness of layer 11 is from 0.5 mil to 2.5 mil which is equivalent to 12.7-63 μm and the thickness of layer 12 is from 0.2 to 3.0 mil which is equivalent to 5-76 μm for layer 12. This teaching implies that the thickness of the multilayer film is from 17.7 to 139 μm and the reference suggested thinner and thicker widths may be employed. Therefore, the thickness taught by the prior art overlaps with the instant claims, unlike applicants assertion that the prior

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art teaches much higher thickness. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. **See MPEP 2144.05 [R-5]**. In any event the prior art suggested thinner thicknesses. The examiner believes that every element of the claims are taught by the combined teachings of the prior art. JP '122 is relied upon for teaching bisoprolol suitable for transdermal delivery and for teaching specific claimed adhesive.

In addition, regarding applicant's arguments of unexpected results of the present invention, it is the examiner's position that the data in the specification regarding properties of the package are not unexpected results and therefore can not rebut prima facie obviousness. The examiner directs applicant's attention to MPEP 716.02 (a). "A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness of the claims at issue." *In re Corkhill*, 711 F.2d 1496, 266 USPQ 1006 (Fed.Cir. 1985). *In Corkhill*, the claimed combination showed an additive result when a diminished result would have been expected. Furthermore, the MPEP states, "Expected beneficial results are evidence of obviousness of a claimed invention, just as unexpected results are evidence of unobviousness thereof." *In re Gershon*, 372 F.2d 535, 538, 152 USPQ 602, 604 (CCPA 1967). Kanios et al. teach their package prevents and controls degradation reactions that resulting from contamination of active material with packaging materials and improves stability of the drug during storage prior to use. The ultimate result of protecting the patch as desired by applicants is achieved by the package taught by the cited prior art.

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Applicants argue that whether taken alone, or in combination, none of the cited references teach or suggest a patch-containing pouch, comprising: a multilayer film having a thickness of from 20 to 100 μm , as recited in claim 7. Applicants argue that neither Kanios, nor the skilled artisan at the time of invention of the presently claimed subject matter, conceived or considered making a pouch having the presently claimed thickness for containing a patch with the presently claimed structure. Any assertion to the contrary could only be made with hindsight, in view of the present specification and claims.

In response to these arguments, the examiner hereby repeats that the claimed thickness of the multilayer film overlaps with that taught by Kanios and Kanios further suggests thinner thickness. The combined teaching of the prior art would reasonably arrive to the present invention comprising stable transdermal system comprising acrylic acid-based adhesive layer containing bisoprolol wherein the patch is packaged in a multilaminate package having the innermost layer of acrylonitrile and outermost layer of terephthalate, wherein the thickness of the multilaminate is 17.7-139 μm and wherein the patch is protected against degradation reactions that resulting from contamination of active material with packaging materials. The examiner believes that the present invention as a whole is taught by the combined teachings of the prior art and not made using hindsight of applicants' disclosure. In any event, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does

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not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The examiner believes that the present invention as a whole as defined by the claims is taught by the combination of the prior art and would have been prima facie obvious in the meaning of U.S.C. 103(a).

7. Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Kanios and JP '122 as applied to claims 7-8, 11-12 above, and further in view of JP 07-132946 ('946).

Applicant Claims

Applicants' claims 13 and 14 further recite an aluminum foil between the polyacrylonitrile layer and the polyethylene terephthalate layer of the packaging material.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

The combined teachings of Kanios and JP '122 are previously discussed in this office action.

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However, the combination of the references does not teach the aluminum foil between the innermost and outermost layers of package as instantly claimed by claims 13 and 14.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

JP '946 teaches packaging for cataplasm using packaging material comprising innermost layer of polyacrylonitrile, outermost layer of polyethylene terephthalate wherein the innermost layer and outermost layer are combined with an aluminum foil layer (paragraphs 001, 004, 0013). The packaging prevent adsorption of active agent to the package and does not cause fall in the drug effect (paragraphs 0014, 0015).

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide transdermal system comprising bisoprolol packaged in a multilaminate package having the innermost layer of acrylonitrile and outermost layer of terephthalate as taught by the combination of Kanios and JP '122, and further add aluminum foil layer between the innermost and outermost layer as taught by JP '946. One would have been motivated to do so because JP '946 teaches that such a multilaminate package prevents adsorption of active agent to the package and does not cause fall in the drug effect. One would reasonably expect formulating transdermal

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system comprising bisoprolol and packaged in a multilaminate package having innermost layer of polyacrylonitrile layer that is combined with an outermost layer of polyethylene terephthalate by an aluminum foil layer wherein the drug is stabilized.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

8. Applicant's arguments filed 09/15/2010 have been fully considered but they are not persuasive.

Applicants repeat the argument regarding the thickness of the multilayer film, and therefore the examiner hereby repeats the response as set forth in this office action.

Applicants further argue that JP '946 does not remedy the deficiencies of Kanios and JP '122 because whether taken alone or together, none of the cited references teach or suggest a patch-containing pouch, comprising: a multilayer film having a thickness of from 20 to 100 μm , as presently claimed.

In response to this argument, it is argued that the multilayer film package with the claimed thickness is taught by the combination of Kanios and JP 122. JP '946 is relied upon for the sole teaching of aluminum foil layer between the two layers of the package for the advantage of prevention of adsorption of active agent to the package

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and for protection against fall in the drug effect. The examiner believes that the present invention as a whole as defined by the claims is taught by the combination of the prior art and would have been prima facie obvious in the meaning of U.S.C. 103(a).

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

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